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MELBOURNE

Melbourne Medical School
Department of Paediatrics

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COVID-19 KIDS RESEARCH EVIDENCE UPDATE

WHAT THE MELBOURNE
CHILDREN'S CLINICIANS,
SCIENTISTS, EPIDEMIOLOGISTS,
AND MEDICAL STUDENTS HAVE
BEEN READING

Update No. 32

17th December 2020



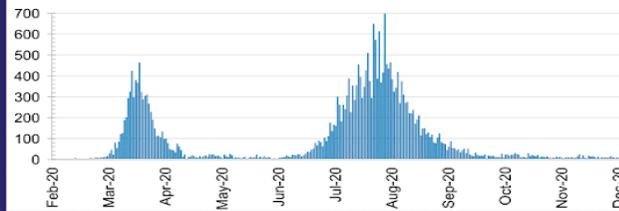
Australian Government
 Department of Health

BE COVIDSAFE

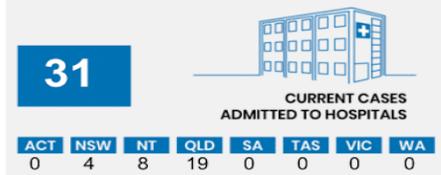
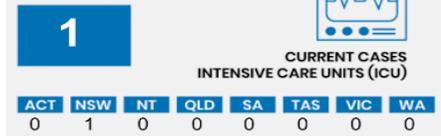
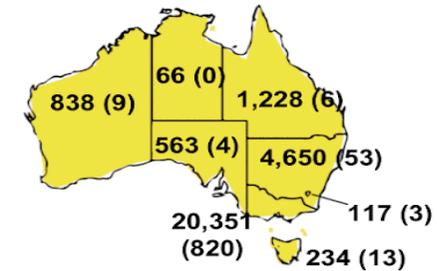
CURRENT STATUS OF CONFIRMED CASES



DAILY NUMBER OF REPORTED CASES



CASES (DEATHS) BY STATE AND TERRITORIES



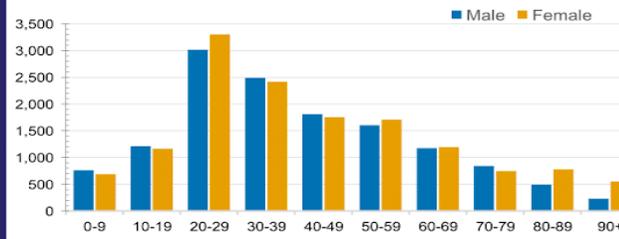
State/Territory	Total Tests	Positive Rate
ACT	126,359	0.1%
NSW	3,622,127	0.1%
NT	76,337	0.1%
QLD	1,398,254	0.1%
SA	769,705	0.1%
TAS	135,294	0.2%
VIC	3,701,454	0.5%
WA	589,756	0.1%

CASES IN AGED CARE SERVICES

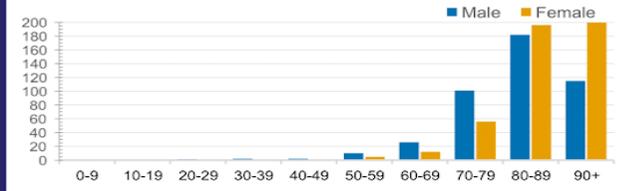
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	2049 [1364] (685)	0	61 [33] (28)	0	1 (1)	0	1 (1)	1986 [1331] (655)	0
In Home Care Recipients	81 [73] (8)	0	13 [13] (0)	0	8 [8] (0)	1 [1] (0)	5 [3] (2)	53 [48] (5)	1 (1)

Cases in care recipients [recovered] (deaths)

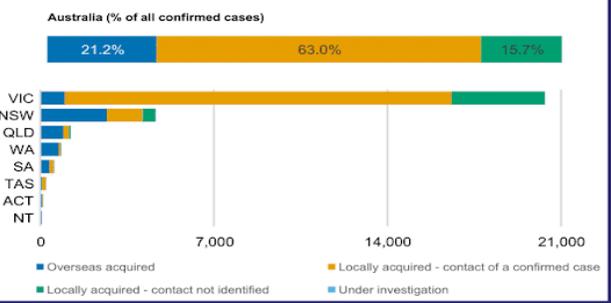
CASES BY AGE GROUP AND SEX



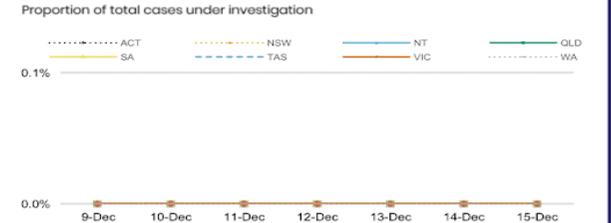
DEATHS BY AGE GROUP AND SEX



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 15 December 2020

This infographic is updated every afternoon based on the data we receive by 3.00pm from states and territories

Source: Australian Government: Department of health [Internet]. 2020 [updated 2020 December 15; cited 2020 December 16]
 Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

GUEST EDITORIAL

Dr Wonie Jahwatanasakul - Paediatrician- Immunisation service RCH,
MD Child and Adolescent Health Program Lead Coordinator,
Department of Paediatrics, The University of Melbourne

What happened to medical education during the COVID-19 pandemic?

For our 32nd edition of the COVID-19 kids' update in Australia, we are in the fortunate position of having no community transmission over the past week, while the virus continues to ravage countries across the world. Medical students from the University of Melbourne and the University of Ottawa have played a vital role in producing our updates over the past months, simultaneously navigating and managing the significant impact on their medical education.

Previous experience with the severe acute respiratory syndrome (SARS) in 2003, saw the effects of lost student placements.(1) As Australia responded to the pandemic by going into lockdown from March 2020, many student placements ceased. Concerns about keeping medical students on placement included: the safety of supervision, limited personal protective equipment, the ease of SARS-CoV-2 transmission, and adaptation to practice change overwhelming clinicians. In Victoria, clinical placement loss was protracted for many months, and social distancing requirements have continued to limit placements. The tension between the need to continue student placements and the safety of their supervision dominated educators' early planning. Final year students were prioritised for clinical placements to ensure graduation, and an intern workforce ready for early deployment in October 2020, if the need arose.

COVID-19 has driven rapid changes in medical education and curricula. The isolation of lockdown, uncertainty of medical education, and loss of casual work incomes have had a significant impact on many students.(2) Anticipating this impact, educators developed and implemented new curricula within weeks, to support students learning and well-being. Online platforms created spaces for students to continue their learning around case discussion with experts, virtual ward rounds, and videoconferencing in a variety of clinical settings. Student assessment was overhauled to ensure it was robust and equitable in new online formats. Clearer communication lines were established between faculty and students to relay the frequent changes. Opportunities for students arose from the public health response, including employment within respiratory screening clinics, training as clinician assistants (in case of workforce impacts from COVID-19), and assisting with public health research.(3)

Clinician educators have collaborated in new ways to redesign medical curricula. The barriers of distance and the ability to deliver remote teaching sessions have made medical education more equitable for all students. How we respond to future threats in healthcare and continue to innovate medical education is important to reflect on. There are many lessons to take from COVID-19, and how we manage the education of medical students when the next threat to our healthcare system eventuates.

I extend a huge thank you to all the students who have worked with us over many months and recognise their enormous contribution to developing this useful resource while continuing their own education in difficult circumstances. It has also been a great pleasure to have worked closely alongside Professor Fiona Russell, Eleanor Neal, and all our regular expert contributors and we look forward to bringing you the next COVID Kids Update in February 2021.

1. Patil NG, Chan Y, Yan H. [SARS and its effect on medical education in Hong Kong](#). *Med Educ*. 2003;37(12):1127-1128. doi:10.1046/j.1365-2923.2003.01723.x
2. Lyons Z, Wilcox H, Leung L, Dearsley O. [COVID-19 and the mental well-being of Australian medical students: impact, concerns and coping strategies used](#). *Australas Psychiatry*. 2020;28(6):649-652. doi:10.1177/1039856220947945
3. Lucey CR, Johnston SC. [The Transformational Effects of COVID-19 on Medical Education](#). *JAMA*. 2020;324(11):1033-1034. doi:10.1001/jama.2020.14136

SELFIES



Wowie
Uahwatarasakul



FIONA RUSSELL



Eleanor
Neal



ALASTAIR
WENG



Ben Watson



Bowen Lim



Celina DiBisio



Charissa
Chan



CHELSEA
HALIBURTON



Dan Lindholm



Dan Lamanna



GRACE NEWMAN



Julia Sweet



Kieren
Fahey



Maria Gladkikh



Rafael
Lee



Rose
Kizhakekara



SAMAR
HIKMAT



Thang Dao



Victoria
Ivankovic

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DISCLAIMER

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Unless specifically stated, the authors do not recommend or endorse any procedures or processes described in this resource.

Response to COVID-19 and any other medical condition at this time is based on science that is new, often uncertain, subject to change, and dependent on context.

Always seek the advice of your physician or another qualified health provider properly licensed to practice medicine or general healthcare in your jurisdiction concerning any questions you may have regarding any information obtained from this publication.

Never disregard professional medical advice or delay in seeking it because of something you have read in this publication. Information obtained in this publication is not exhaustive and does not cover all possible manifestations of COVID-19 nor its interaction with other conditions, diseases, ailments, or their treatment.

The Owners of this resource do not wish to use this resource as a means of communication with the general public (i) regarding questions or issues of a medical nature; (ii) to establish physician-patient relationships. Email communications regarding such matters will not be responded to and will be discarded unread.

HIGHLIGHTS

- > Compared with older adults, children and young adults are less likely to manifest with severe or fatal symptoms of COVID-19 due to two broad categories of factors: those that put adults at higher risk and those that protect children.
- > Detectable levels of antibodies to SARS-CoV-2 remain present for at least 62 days in infected children which is consistent with the kinetics of adult antibody titres.
- > In the U.K., a study found no increased risk of severe COVID-19 outcomes amongst adults living with children compared to those living with no children.
- > A retrospective cohort study of 135,794 U.S. paediatric patients (<25 years) showed that SARS-CoV-2 infection rates were low, with typically mild clinical manifestations. However, minority race/ethnicity, increasing age and non-respiratory chronic illness were associated with infection.
- > Since the onset of the pandemic, the reduction in outpatient services, diagnosis, treatment, and immunisation have all put children at an increased risk of severe and potentially fatal infections, including pneumonia. However, the COVID-19 pandemic and lessons learned from it (such as hand washing, vaccine confidence, and increased supplies of oximeters) may provide an opportunity to reduce future deaths from childhood pneumonia.
- > Vulnerable children and young people (CYP) have been disproportionately impacted by the COVID-19 pandemic. A collective effort is needed by healthcare workers, governments and researchers to address health inequity and create sustained well-being for vulnerable CYP.
- > The COVID-19 pandemic has disrupted immunisation programs around the world, potentially increasing life-threatening vaccine-preventable diseases. Pakistan, a country struggling to eradicate polio, has endured the suspension of all vaccination programs since April 2020 due to the COVID-19 pandemic, resulting in a missed vaccination effort to over 40 million children.
- > Higher levels of COVID-related stress and caregiver reported child psychosocial concerns were independently associated with worse mental health symptoms in caregivers.
- > The SARS-CoV-2 pandemic has had far-reaching implications, including changes in societal stressors and healthcare delivery, which may alter preterm birth risk.
- > A summary report from the Scottish Advisory Sub-Group on Education and Children's Issues was recently published and, based on available evidence, concludes that the benefits to schools remaining open outweigh the risks.
- > A case report of a childcare centre exposure involving a pre-symptomatic four-year-old boy with SARS-CoV-2, no transmission occurred among many contacts
- > Summary of public health strategies recommended by the US CDC to reduce COVID-19 transmission

- > A single centre retrospective study in the USA, including 71 children testing positive for SARS-CoV-2 showed no child to adult transmission and one case of a child-to-child transmission.
- > The duration of viable SARS-CoV-2 virus is relatively short - SARS-CoV-2 titres in the upper respiratory tract peak in the first week of illness. Isolation practices should be commenced with the start of the first symptoms to contain SARS-CoV-2 effectively.
- > Children have similar probability as adults to become infected by SARS-CoV-2 in quarantined family households but remain mostly asymptomatic once infected.
- > Despite the adults travelling in the same vehicle with their COVID-positive child/children, staying in the same room during the mandatory quarantine period, and in the hospital (without adequate PPE), most of the parents involved in such index cases remained COVID-19 negative.
- > The mRNA-1273 vaccine produced high levels of binding and neutralising antibodies that declined slightly over time but remained elevated in all participants 3 months after booster vaccination.
- > Phase 2/3 trials of the ChAdOx-1 vaccine candidate reveal promising safety and immunogenicity data in both younger and older adults.
- > Whilst the global solidarity in ensuring equitable access to vaccines through the COVAX initiative is promising, several challenges threaten to compromise access for all.
- > Phase 3 trial of the mRNA-1273 vaccine at two months follow-up shows 94.1% efficacy against COVID-19 infection and 100% efficacy against severe COVID-19 infection.

PAPERS OF INTEREST

- > [Coronavirus \(COVID-19\) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19](#)
- > [Correlates of protection against SARS-CoV-2 in rhesus macaques](#)
- > [EMG/SPI-B: Mitigating risks of SARS-CoV-2 transmission associated with household social interactions, 26th November 2020](#)
- > [Factors associated with positive SARS-CoV-2 test results in outpatient health facilities and emergency departments among children and adolescents aged 18 years – Mississippi, September – November 2020 | MMWR](#)
- > [Heterogeneity in transmissibility and shedding SARS-CoV-2 via droplets and aerosols](#)
- > [Immune responses to SARS-CoV-2 in three children of parents with symptomatic COVID-19](#)
- > [Immunity to SARS-CoV-2 and the concept of an Immunity Certificate.](#)
- > [Implementing Mitigation Strategies in Early Care and Education Settings for Prevention of SARS-CoV-2 Transmission – Eight States, September–October 2020](#)
- > [NERVTAG: Risk assessment of SARS-CoV-2 variants that have been selected in mink, 12th November 2020](#)
- > [No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2](#)
- > [Pre-existing T cell-mediated cross-reactivity to SARS-CoV-2 cannot solely be explained by prior exposure to endemic human coronaviruses](#)
- > [Priorities for the child public health response to the COVID-19 pandemic recovery in England](#)
- > [Repurposed Antiviral Drugs for Covid-19 – Interim WHO Solidarity Trial Results](#)
- > [Research and analysis TFC: Children and transmission, 4th November 2020](#)
- > [Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine - Nick Baxter](#)
- > [SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England](#)
- > [SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis](#)
- > [Secondary transmission of COVID-19 in preschool and school settings in northern Italy after their reopening in September 2020: a population-based study](#)
- > [Why COVID-19 strengthens the case for a dedicated financing mechanism to scale up innovation in women's, children's, and adolescents' health](#)

EPIDEMIOLOGY & PUBLIC HEALTH

Thomas Hill – 3rd Year Medical Student,
Department of Paediatrics, University of Melbourne

COVID-19 pandemic: The impact on vulnerable children and young people in Australia

<https://onlinelibrary.wiley.com/doi/full/10.1111/jpc.15169>

- > The study aimed to describe the reasons for the vulnerability of children and young people (CYP) during the pandemic and to determine which health professional actions would mitigate these effects.
- > A rapid review of the literature, as well as group discussion, identified eight groups of CYP that were particularly vulnerable to the impact of COVID-19: CYP with disabilities, mental health conditions or chronic disease; CYP facing financial hardship; CYP within the child protection system; Aboriginal and Torres Strait Islander CYP; migrant and refugee CYP; CYP in residential care; rural CYP; and isolated CYP.
- > The long-term social and economic downturn will continue to impact CYP experiencing financial hardship, Aboriginal and Torres Strait Islander CYP, CYP from migrant and refugee backgrounds, CYP in residential care, rural CYP and those who are socially isolated.
- > Aboriginal and Torres Strait Islander CYP are faced with the additional challenges of limited access to extended family, cultural connections and community events, and increased health risks for family members due to intergenerational living.
- > Intervention is required by healthcare workers, governments and researchers.
- > Healthcare workers should use telehealth with careful consideration when consulting with vulnerable CYP; should use integrated care with allied health, and should be vigilant and prepared to respond to increased child protection and family violence cases.
- > Governments should increase spending on health services; develop clear policies on prioritisation of care for patients on waiting lists and outpatient mental health services, and ensure adequate financial and social support for families and CYP financially impacted by the pandemic.
- > Researchers should provide agency to families and CYP by incorporating their voices in actions and considerations that involve them; provide accessible and evidenced based information in multiple formats, and undertake research to understand the impact of the pandemic on CYP from all backgrounds.
- > Collectively this experience may be used to 'Build it Better' and optimise health equity and sustained well-being for vulnerable CYP.

Reviewed by: Dr Claire von Mollendorf

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Association between living with children and outcomes from COVID-19: an OpenSAFELY cohort study of 12 million adults in England (not peer reviewed)
<https://www.medrxiv.org/content/10.1101/2020.11.01.20222315v1>

- > A prospective cohort study conducted in England from 1st February to 3rd August 2020 to determine whether the risk of SARS-CoV-2 infection and severe outcomes differed between adults living in households with and without children. Severe outcomes were defined as hospitalisation, ICU admission or death due to COVID-19.
- > Approximately 12 million adults aged ≥18 years living in England and registered in a G.P. practice for three or more months were included.
- > Among 9,157,814 adults aged ≤ 65 years:
 - Living with children aged 0-11 years was not associated with an increased risk of SARS-CoV-2 infection, COVID-19 related hospitalisation or ICU admission and was associated with a reduced risk of death from COVID-19 (HR 0.75 [95% CI 0.62 - 0.92]).
 - Living with children aged 12-18 years was associated with a slightly increased risk of SARS-CoV-2 infection (HR 1.08 [95% CI 1.03 - 1.13]) but was not associated with severe outcomes.
- > Among 2,567,671 adults aged > 65 years:
 - Living with children of any age was not associated with any of the COVID-19 related study outcomes.
- > The risks described did not differ between the periods before and after school closures.
- > Limitations:
 - SARS-CoV-2 infection is mainly based on swab tests taken in community testing centres and healthcare settings which is likely influenced by testing of people in high-risk jobs.
 - The study was not able to adjust for confounding by previous comorbidities that affect the ability to have children and subsequent risk of severe COVID-19 outcomes.
 - Assuming a constant relationship for infections between people through clustering at the household level, rather than transmission models.
- > Conclusion: Living with children did not increase the risks of severe COVID-19 related outcomes amongst adults. These findings have major implications for informing health policies regarding school closures during the COVID-19 pandemic.

Reviewed by: Dr Claire von Mollendorf

Rose Noble Kizhakekara – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Assessment of 135 794 pediatric patients tested for severe acute respiratory syndrome coronavirus 2 across the United States

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773298>

- > Retrospective cohort study of electronic records of 135,794 patients younger than 25 years who were tested for SARS-CoV-2 from 1st January to 8th September 2020 in seven paediatric health systems in the United States.
- > 4% (n=5,374) of the study population tested for SARS-CoV-2 were infected.
- > Epidemiological results:
 - Compared with White patients, patients of Black, Hispanic and Asian race/ethnicity had lower rates of testing but were significantly more likely to test positive.
 - Other factors associated with increased risk of infection included older age (age > five years), public payer, outpatient (vs. inpatient) testing and emergency department (vs. inpatient) testing.
 - Non-malignant chronic disease was associated with a lower likelihood of testing, and pre-existing respiratory conditions were associated with a lower risk of infection.
 - There was a higher risk of infection in the following diagnosis groups; malignant disorders, cardiac disorders, endocrinologic disorders, gastrointestinal disorders, genetic disorders, hematologic disorders, musculoskeletal disorders, mental health disorders and metabolic disorders.
- > Disease outcomes:
 - 7% (359 of 5,374 patients with positive test results) were hospitalised for respiratory, hypotensive or COVID-19-specific illness (met criteria for severe disease).
 - Of those hospitalised, 99 (28%) required intensive care services and 33 (9%) required mechanical ventilation.
 - Eight patients with positive test results died (case fatality rate of 0.2%).
 - The number of patients with a diagnosis of Kawasaki disease in early 2020 was 40% lower (259 vs 433 and 430) than in 2018 or 2019.
 - Factors associated with severe COVID-19 in those who tested positive included Black race/ethnicity, age younger than one, age 12 to 17 years, age 18 to 24 years, history of public insurance and presence of the progressive condition. Specifically, endocrinologic, metabolic and malignant disorders were associated with increased risk of severe illness.
- > Limitations: The study used viral genome detection, but this excludes patients with COVID-19 when viral testing was not readily available at all sites. There may also be differing guidelines for testing across different institutions for asymptomatic patients so the associations between chronic illness and infection may reflect practice patterns rather than disease biology.

Reviewed by: Dr Claire von Mollendorf

Julian Loo Yong Kee - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Kinetics and seroprevalence of SARS-CoV-2 antibodies in children
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30884-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30884-7/fulltext)

- > Results of a second round of antibody testing in children from a prospective multicentre cohort study in the United Kingdom.
- > 2-15 year old children were recruited between 16th April and 3rd July 2020 at five sites, with follow-up between 26th July and 15th August 2020.
- > The median time between initial and follow-up visits was 62 days (IQR 52-70; range 43-81).
- > Similar seroprevalence at recruitment and follow-up (6.9% and 7.66% respectively).
- > Significant increase in antibody titre was observed in the 45 participants with reactive antibody tests at recruitment.
- > Detectable levels of antibodies to SARS-CoV-2 remain present for at least 62 days in children which is consistent with available data on adult antibody titres.

Reviewed by: Dr Claire von Mollendorf

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Summary of guidance for public health strategies to address high levels of community transmission of SARS-CoV-2 and related deaths, December 2020
<https://www.cdc.gov/mmwr/volumes/69/wr/mm6949e2.htm>

Recommended public health strategies by the US Centers for Disease Control and Prevention (CDC) to reduce COVID-19 transmission:

- > The universal use of face masks:
 - Is most important in indoor settings and outdoor settings where the physical distance of ≥ 6 feet cannot be maintained.
 - Should be considered within households if a member is infected or has had potential exposure to a COVID-19 case.
- > Maintaining physical distancing of ≥ 6 feet and limiting in-person contacts.
 - Consider the use of physical barriers and visual reminders to promote adherence to physical distancing.
- > Avoiding non-essential indoor spaces and crowded outdoor settings.
 - Consider transitioning to telework and restricting the number of people in indoor/outdoor spaces.
- > Increased testing and prompt contact tracing to rapidly identify and isolate infected people and their close contacts.

- In addition to testing symptomatic people and those with known SARS-CoV-2 exposure, it is recommended to routinely test individuals with many interactions (e.g., workers in crowded worksites) and those interacting with high-risk groups (e.g., staff in nursing homes).
- Test results should be promptly reported to the individual tested and to public health authorities to promote rapid isolation and contact tracing.
- > Protecting people at risk for severe SARS-CoV-2 illness or death (including elderly people and those with underlying medical conditions).
 - Long term facilities should implement infection control measures and routine screening of workers and residents to identify and isolate infected individuals.
 - People at high risk and those that share a household with them are encouraged to minimise non-essential interaction with non-household members.
- > Protecting essential workers by providing adequate personal protective equipment and implementing safe workplace practices.
- > Travelling:
 - International and domestic travel should be postponed where possible. If people need to travel, they should be tested before leaving and again after arriving.
 - Travellers should stay at home or reduce unnecessary activities before and after travelling and should comply with wearing masks, hand hygiene and physical distancing.
- > Increasing room air ventilation, frequent disinfection of touched surfaces and enhanced hand hygiene (using soap and water or alcohol-based hand sanitiser).
- > Vaccines:
 - Plans should be implemented to distribute and administer vaccines when they become available and are approved for use to ensure high community coverage.
 - Educating the public that they must still comply with infection control measures (e.g., hand hygiene, face masks) until there is adequate community vaccination coverage.

Reviewed by: Professor Fiona Russell

GLOBAL HEALTH

Contain This: The Latest in Global Health Security

<http://containthis.buzzsprout.com/>

Daniel Lamanna - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Impact of COVID-19 on polio vaccination in Pakistan: a concise overview

<https://onlinelibrary.wiley.com/doi/10.1002/rmv.2190>

The COVID-19 pandemic has disrupted immunisation programs around the world, potentially increasing life-threatening vaccine-preventable diseases. Pakistan, a country struggling to eradicate polio, has endured the suspension of all vaccination programs since April 2020 due to the COVID-19 pandemic, resulting in a missed vaccination effort to over 40 million children. The staff trained for vaccination against poliomyelitis have been redirected towards the fight against the COVID-19 pandemic.

- > There is no report of wild poliovirus (WPV) cases outside of Pakistan and Afghanistan since 2015.
- > In 2018, there were 33 global cases of WPV-1 reported of which 12 (36%) were from Pakistan and 21 (64%) from Afghanistan.
- > In 2019, there were 176 global cases of WPV-1 reported of which 147 (84%) were from Pakistan, and 29 (16%) were from Afghanistan.
- > It is possible that the number of cases of polio will increase, and subsequently add pressure to the already overburdened health sectors across Pakistan - vaccination efforts should be resumed as soon as possible to reduce the possibility of unravelling the progress made against polio over the last 30 years.
- > A delay in polio vaccination may not have an immediate impact; however, there may be long-term consequences as an increase in polio cases in Pakistan may result in the global export of disease.
- > Given the complexity of this issue, public health figures must balance the fight against COVID-19 with the need to mitigate the effects of re-emerging viral disease as multi-infection could make the situation worse, especially in underdeveloped countries.
- > Similar to the climate-change crisis, the COVID-19 pandemic could be regarded as a child-rights crisis because it will have a life-threatening impact on those children who require immunisations, both now and in the long-term.

Reviewed by: Professor Julie Bines

Rebecca Seliga – 3rd Year Medical Student, University of Ottawa

Leveraging the COVID-19 response to end preventable childhood deaths from pneumonia

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32348-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32348-5/fulltext)

- > This commentary published to mark World Pneumonia Day (12th November 2020), emphasised the opportunity to build on the momentum created by the COVID-19 pandemic to address other critical preventable illnesses such as global childhood pneumonia.
- > Despite improvements over the past decade, pneumonia is still the leading infectious cause of child deaths, resulting in >800,000 deaths each year.
- > While children have less severe COVID-19-related illness than adults, secondary impacts such as food shortages and reduced access to care have resulted in additional deaths amongst children under five years old. Data suggest that 1/3 of these preventable deaths could be from pneumonia and newborn sepsis.
- > Since the onset of the pandemic, the reduction in outpatient services, diagnosis, treatment, and immunisation have all put children at an increased risk of severe and potentially fatal infections.
- > But there is the potential to use some of the measures introduced as part of the COVID-19 response to impact other health outcomes, such as:
 - Mask wearing, social distancing and hand hygiene reduce not only COVID-19 transmission but also that of other pathogens.
 - Increased distribution of pulse oximeters and other oxygen equipment, and support and training for primary health care staff, have the potential to improve the diagnosis and treatment of childhood hypoxemia and pneumonia.
 - Greater acceptance of the value of vaccines in protecting lives. This could improve routine childhood vaccination.
- > In January 2020, The Global Forum on Childhood Pneumonia endorsed six strategic actions to reduce childhood pneumonia deaths:
 1. Develop and implement pneumonia control strategies
 2. Prioritise vulnerable populations
 3. Finance pneumonia control and treatment adequately
 4. Accelerate breakthrough innovations
 5. Track progress with transparency, accountability, and inclusiveness
 6. Strengthen partnerships
- > This commentary emphasised the importance of:
 - Routine paediatric health services should be maintained both during and after the pandemic.
 - Ensure that health facilities across the globe are equipped with the basic needs to support their communities.

- Increase diagnostic and treatment services for respiratory infections.
- Plan to redeploy oxygen supplies to newborn and paediatric healthcare settings after the pandemic.

Reviewed by: Professor Julie Bines

IMMUNOLOGY

Benjamin Watson – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Functional SARS-CoV-2-specific immune memory persists after mild COVID-19
<https://www.sciencedirect.com/science/article/pii/S0092867420315658>

- > Most infected individuals experience mildly symptomatic COVID-19, but it is unknown whether this can induce persistent immune memory that could contribute to immunity.
- > This study assessed SARS-CoV-2-specific immune responses at 1- and 3-months post-symptom onset in individuals that had experienced mild COVID-19 individuals (N=15, median age: 47); their immune responses were compared with healthy controls (N=17, median age: 45).
- > Major findings: Compared with healthy controls, mild COVID-19 induces:
 - persistent, neutralising anti-SARS-CoV-2 IgG antibody.
 - sustained enrichment of RBD-specific IgG+ memory B cells (CD21+CD27+, classical memory B cells), and a higher number of T-bet+ RBD-specific MBCs.
 - durable, functional memory CD4+ T cells.
 - Enhanced expression of ICOS and CD40L.
 - Higher number of CXCR5-expressing circulating T follicular helper cells.
 - Significant higher numbers of activated, cytokine-producing cells in memory T cells (IL-2 and IFN-gamma).
 - SARS-CoV-2-specific memory B cells that can express neutralising antibodies.
 - Formed and sustained multiple components of immune memory responses.
- > Recovered mild COVID-19 individuals formed a multifaceted immune defence, suggesting that attenuated virus vaccines are likely to be similarly successful in eliciting a functional immune memory response.
- > Limitations: Small sample size; unclear if the results represent the immune memory response after asymptomatic or severe disease; whether the immune memory responses persist > 3 months is unknown; protection from reinfection unknown and if any of these immune parameters correlate with protection.

Reviewed by: Dr Ryan Toh

MENTAL HEALTH

Professor Sharon Goldfeld - Director, Centre for Community Child Health, Royal Children's Hospital; Theme Director Population Health and CoGroup Leader Policy and Equity, Murdoch Children's Research Institute; Professor, Department of Paediatrics, Faculty of Medicine Dentistry and Health Sciences, University of Melbourne, and Dr Elodie O'Connor, Research Assistant, Policy and Equity, Population Health, Murdoch Children's Research Institute

Growing up in the shadow of COVID-19

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30349-7/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30349-7/fulltext)

The U.K. Government have not adequately considered young people in their response to COVID-19.

- > The closure of schools, nurseries, and outdoor play spaces, and reduced access to health services, have widened existing disparities in child health.
- > While 74% of children at private schools had access to full days of teaching during the lockdown, only 38% of state school students had access to this.
- > There has been an increase in the number of children and young people with a probable mental disorder, with many reporting sleep problems and loneliness.
- > During the second wave, the needs of children must be considered; services should remain accessible, schools should remain open for as long as possible, and if closed, vulnerable children should be given additional support (e.g., free meals, access to laptops and internet).
- > Before the pandemic, there was evidence of widening inequalities and poorer child mental health; the Government's handling of the pandemic has exacerbated these issues.
- > Long-term investment in both prevention and early intervention is needed to help children and young people recover from the indirect effects of COVID-19.
 - This includes prioritising: early childhood intervention, mental health support in schools, catch-up vaccination programs, social care for children from vulnerable families, and increased funding to reduce child poverty.

Thomas Hill – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Risk and resilience of well-being in caregivers of young children in response to the COVID-19 pandemic

<https://academic.oup.com/tbm/advance-article/doi/10.1093/tbm/ibaa124/6001694>

- > The current American-based study utilised online surveys to evaluate the effects of the COVID-19 pandemic on family functioning and mental health in a racially, ethnically and linguistically diverse group of caregivers (N = 286) with children ages birth to five.
- > Descriptive statistics were also reported from the conducted surveys. Of note:
 - Caregiver Mental Health Symptoms: 72% reported increased anxiety, 46% reported increased sadness/depression, 39% reported sleep disturbances, and 34% reported increased anger.
 - Managing family needs: 38% of caregivers reported problems with their child's behaviour, and 42% reported concerns about their child's schooling from home.
 - 92% of caregivers reported confidence in upholding safety recommendations issued by the CDC.
- > Path analysis was used to partially quantitatively assess the conceptual model of family risk and resiliency designed by Prime et al. (2020). Authors assessed eight hypothesised paths with three regression analyses.
- > Of the eight hypothesised paths, four were statistically significant. Results are presented as standardised (β) path coefficients and standard errors. Significance was set at $P < 0.05$.
 - Caregiver COVID-related Stress had a positive association with Caregiver Mental Health Symptoms ((0.45(0.05)).
 - Caregiver COVID-related Stress had a negative association with COVID-related Caregiver Self-Efficacy ((-0.19(.09)).
 - COVID-related Caregiver Self-Efficacy had a negative association with Caregiver Mental Health Symptoms ((-0.19(.05)).
 - Child Psychosocial Problems had a positive association with Caregiver Mental Health Symptoms ((0.21(.07)).
- > Limitations: cross-sectional design only represents views of families in the initial stages of the pandemic in the USA; predisposing factors were not included in the analysis; not all surveys had been previously validated due to the rapid onset of the pandemic.

Reviewed by: Professor David Coghill

PERINATAL HEALTH

Nicholas Wu – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Stillbirths during the COVID-19 pandemic in England, April-June 2020

<https://jamanetwork.com/journals/jama/fullarticle/2774088>

- > Although pregnant women are at increased risk of infectious diseases, little is known about the risk of COVID-19 to unborn children. Data has been sparse with one hospital in London reporting an increase in stillborn babies during the pandemic compared to a similar period the year before. Therefore, national and regional hospitalisation data in England was used to assess the risk of stillbirths during the COVID-19 pandemic.
- > National Health Service (NHS) hospital admissions for mothers experiencing a stillbirth (foetal death > 24 weeks' gestation) were assessed from 1st April 2019 - 30th June 2020 and compared to stillbirth rates for the same period in 2019.
- > From 1st April to 30th June 2020, there were 543 stillbirths, compared with 565 stillbirths for the same period in the previous year (incidence rate ratio, 1.02 [95% CI 0.91-1.15]; P = 0.69).
- > No evidence of any increase in stillbirths regionally or nationally during the COVID-19 pandemic in England when compared with the same months in the previous year.
- > Limitations: No data available on SARS-CoV-2 infection status, maternal sociodemographic characteristics, or access to care for the cohort.

Reviewed by: Professor Suzanne M Garland.

Celina DeBiasio - 3rd Year Medical Student, University of Ottawa

Changes in preterm birth phenotypes and stillbirth at 2 Philadelphia hospitals during the SARS-CoV-2 pandemic, March-June 2020

<https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2020.20991>

- > The authors examined a diverse United States cohort of two Penn Medicine hospitals in Philadelphia to determine if preterm birth, spontaneous preterm birth, medically indicated preterm birth, and stillbirth rates have changed during the SARS-CoV-2 pandemic.
- > Using Geobirth, the authors compared preterm birth, spontaneous preterm birth, medically indicated preterm birth, and stillbirth rates among singleton pregnancies during the pandemic period (March-June 2020) with the same months in 2018 and 2019 (pre-pandemic). They also adjusted for the birth month, age, parity, body mass index, race/ethnicity, marital status, smoking, and insurance status.
- > A total of 8867 singletons, live-born deliveries were recorded March through June of 2018, 2019, and 2020 (42% non-Hispanic Black, 37% non-Hispanic White, and 21% other race/ethnicity); 2992 deliveries occurred during the pandemic period, including 283 preterm births and 15 stillbirths.

- > In the two hospitals, universal SARS-CoV-2 testing began on 1st April 2020, and 13th April 2020. Among 86 patients with test results positive for SARS-CoV-2, the preterm birth rate was 11.6% (n = 10; 6 spontaneous and four medically indicated preterm births), and there was one stillbirth.
- > This study did not detect significant changes in preterm or stillbirth rates during the SARS-CoV-2 pandemic in a racially diverse urban cohort from two Philadelphia hospitals.
- > Limitations: an examination of a single health system, short epochs, limited representation of other races/ ethnicities, few stillbirths, and potential for change in delivery hospital choice during the pandemic.

Reviewed by: Professor Suzanne M Garland

SCHOOLS

Rebecca Seliga – 3rd Year Medical Student, University of Ottawa

Coronavirus (COVID-19): advisory sub-group on education and children’s issues: evidence on children, schools, early learning and childcare settings and transmission- summary report

<https://www.gov.scot/news/coronavirus-covid-19-in-schools/>

- > This government report from Scotland looks at the risks posed by SARS-CoV-2 and compares them to the benefits of children being able to attend school.
- > It concludes that the benefits from schools remaining open outweigh the risks. Some key points from which they drew this conclusion include:
 - The overall rate of coronavirus-related sickness amongst school children in Scotland is very low (around 0.1%).
 - Viral transmission within schools has not been proven to significantly increase infection rates among children.
 - The rate of COVID-19 positivity in teachers is similar to people of the same age bracket working in other professions.
 - Closing schools is detrimental to children’s well-being, especially children who are most vulnerable.
- > To protect the well-being of children, it is important that robust public health measures are implemented in order to reduce community transmission.

Reviewed by: Professor Fiona Russell

TRANSMISSION

Chan Ying Zhen Charissa - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Aerosol emission and superemission during human speech increase with voice loudness

<https://www.nature.com/articles/s41598-019-38808-z>

- > This study used an aerodynamic particle sizer (APS) placed in a laminar flow hood to characterise the number and size distribution of particles emitted by individual human volunteers. At the same time, they performed various vocalisations and breathing activities.
- > Rate of particle emission during normal human speech is positively correlated with the loudness of vocalisation (vocalisation amplitude), ranging from approximately 1 to 50 particles per second (0.06 to 3 particles per cm³) for low to high amplitudes. This is regardless of language spoken: English, Spanish, Mandarin or Arabic.
- > No significant impact of temperature or humidity were found on either the particle emission rate or the mean particle size.
- > Particles emitted during various types of breathing versus speech demonstrates that even quiet speech yields significantly more particles than normal breathing. This is because the particles on average are larger, and thus could potentially carry a larger number of pathogens, and much greater quantities of particles are emitted compared to breathing, thus increasing the odds of infecting nearby susceptible individuals.
- > A small fraction of individuals behave as “speech super emitters”, consistently releasing an order of magnitude more particles than their peers.
- > The phenomenon of speech super mission cannot be fully explained either by phonic structures or the amplitude of speech.
- > Other unknown physiological factors, varying dramatically among individuals, could affect the probability of respiratory infectious disease transmission, and also help explain the existence of superspreaders who are disproportionately responsible for outbreaks of airborne infectious disease.

Reviewed by: Dr Lien Anh Ha Do

Natalie Commins - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Childcare exposure to severe acute respiratory syndrome coronavirus 2 for 4-year-old pre-symptomatic child, South Korea

https://wwwnc.cdc.gov/eid/article/27/2/20-3189_article

- > A case report of a childcare centre exposure involving a pre-symptomatic four year old boy with SARS-CoV-2 from South Korea, during the period 19th - 21st February.
- > The child developed a fever on 22nd February and a cough two days later, PCR performed on 27th February confirmed SARS-CoV-2 infection.
- > He attended his child-care centre for two days whilst pre-symptomatic and was likely exposed to SARS-CoV-2 by his grandmother.
- > He attended several classes with 13 other children and two teachers and caught school transport with approximately 20 other children and several adults.
- > All adults wore masks at the child-care centre, but mask-wearing by children was inconsistent.
- > 190 potential contacts were identified (154 children and 36 adults), with 44 of these contacts being classified as close contacts.
- > All potential contacts returned negative test results. Two patients developed a cough after initial testing but were still negative on repeat PCR.
- > All 190 contacts received D8/D9 PCR testing for SARS-CoV-2.
- > Children make up 2.2-6.7% of SARS-CoV-2 cases. The rates of the child-to-child transmission in child-care centres vary according to location and local public health responses.
- > However, the literature to date suggests that child to child SARS-CoV-2 transmission in child-care settings is uncommon.

Reviewed by: Dr Lien Anh Ha Do

Jun Hua Bowen Lim - 3rd Year Medical student,
Department of Paediatrics, The University of Melbourne

Characteristics and timing of initial virus shedding in severe acute respiratory syndrome coronavirus 2, Utah, USA

<https://doi.org/10.3201/eid2702.203517>

- > SARS-CoV-2 transmission can occur prior to symptom onset, and viral shedding can continue beyond symptom resolution.
- > The authors aimed to describe how household contacts' exposure to an index patient affected SARS-CoV-2 detection and progression of viral shedding.
- > Intensive early monitoring was performed through daily specimens collected from five households four days (median) after symptom onset in the index case.
- > The secondary transmission was seen in two of the five households, and all (7 of 7) household contacts in the two households contracted SARS-CoV-2.
- > It was noted that positive contacts had mild non-specific symptoms prior to their first positive test.

- > Shedding of the SARS-CoV-2 virus might occur early in the disease course before symptom onset and clinical diagnosis, or it could happen when symptoms are mild or even absent.
- > Unlike the other three households, the two households where transmission occurred did not implement household-level isolation practices, possibly due to childcare needs.
- > The findings suggest that household-level isolation practices can prevent transmission, and specific recommendations were outlined by the authors.

Reviewed by: Professor Fiona Russell

Maria Gladkikh – 3rd Year Medical Student, University of Ottawa

Susceptibility to SARS-CoV-2 infection among children and adults: a seroprevalence study of family households in the Barcelona Metropolitan Region, Spain (pre-print)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7717181/pdf/ciaa1721.pdf>

- > This cross-sectional seroprevalence study prospectively recruited volunteer families to assess the seroprevalence of SARS-CoV-2 infection in children and adult contacts living with 1st-reported PCR-positive adult cases in quarantined family households.
- > A total of 381 family households (381 first-reported PCR-positive adult cases) were enrolled.
- > SARS-CoV-2 infection seroprevalence rates were 17.6% (118/672) in children and 18.7% (77/335) in adults. Contact age group, contact sex, smoking habits of family members, and household occupancy rate were not found to be significantly associated with SARS-CoV-2 seroprevalence.
- > Among first-reported cases, seropositivity rates varied from 84.0% in adults previously hospitalised and tested within six weeks since the first positive PCR result to 31.5% in those not hospitalised and tested after that lag time.
- > Contact age group, contact sex, smoking habits of family members, and household occupancy rate were not found to be significantly associated with SARS-CoV-2 seroprevalence.
- > The use of the public instead of private transportation to go to school before home confinement came into force was strongly associated with children being seropositive (33.3 vs. 14.9%).
- > Nearly all (99.9%) positive paediatric contacts were asymptomatic or had mild symptoms.
- > Limitation: impossible to discern whether the cases initially identified were the first family members to become infected; imperfect sensitivity of the rapid lateral flow assay (to detect IgG/IgM).
- > Conclusion: children have similar probability as adults to become infected by SARS-CoV-2 in quarantined family households but remain mostly asymptomatic once infected.

Reviewed by: Professor Fiona Russell

Grace Newman – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

SARS-CoV-2 transmission in an urban community: the role of children and household contacts

<https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa158/6007439>

- > A single centre retrospective study in Detroit, Michigan. 38% of the population in Detroit lives in poverty with many residents not having access to reliable employment, education, housing, food and healthcare.
- > The study included 71 children who tested positive for SARS-CoV-2 via nasopharyngeal swab and PCR assay or serum antibody testing at The Children’s Hospital of Michigan.
- > A retrospective chart review of positive children determined the presence or absence of a sick contact. Patients were also contacted six weeks after discharge to identify subsequent sick contacts. A sick household contact (HHSC) was defined as someone who lives with the child that either tested positive or had symptoms suggestive of COVID-19.
- > 30 children identified a sick household contact prior to the onset of the child’s symptoms, including 25 who had a contact that had tested positive for SARS-CoV-2.
- > Follow up phone calls were completed for 61% of families. There was no reported illness in any household contact up to 6 weeks after the child became ill.
- > There was no evidence of child-to-adult transmission. There was one case of child-to-child transmission.
- > A parent was the most common index HHSC.
- > This study reported that a smaller proportion of children were infected inside familial clusters compared to other studies, which may suggest that children in this study were more likely to have been infected as a result of community transmission rather than household transmission. This may be due to difficulties adhering to strict quarantine and social distancing in an urban population.
- > Limitations: Small sample size, risk of recall bias when phoned six weeks after admission and asked to recall illness in contacts, 1/3 of the families could not be reached for follow up, household contact may have been asymptomatic and not tested.

Reviewed by: Dr Celeste Donato

Maria Gladkikh – 3rd Year Medical Student, University of Ottawa &
Benjamin Watson – 4th Year Medical Student, Department of
Paediatrics, The University of Melbourne

SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis

[https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247\(20\)30172-5/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30172-5/fulltext)

- > This systematic review and meta-analysis characterised viral load dynamics, duration of viral RNA shedding, and viable virus shedding of SARS-CoV-2 in various body fluids, and compared these dynamics to those of SARS-CoV and MERS-CoV.
- > 79 studies (5340 patients) on SARS-CoV-2, eight studies (1858 patients) on SARS-CoV, and 11 studies (799 patients) on MERS-CoV were included.
- > Mean duration of SARS-CoV-2 RNA shedding was 17.0 days (95% CI 15.5-18.6) in the upper respiratory tract, 14.6 days (95% CI 9.3-20) in the lower respiratory tract, 17.2 days (95% CI 14.4-20.1) in stool, 16.6 days (95% CI 3.6-29.7) in serum samples.
- > Maximum shedding duration of SARS-CoV-2 was 83 days in the upper respiratory tract, 59 days in the lower respiratory tract, 126 days in stools, 60 days in serum.
- > Pooled mean SARS-CoV-2 shedding duration was positively associated with age (slope 0.304 [95% CI 0.115-0.493]; $P = 0.0016$) but not sex ($P = 0.28$). There was a positive but non-significant association between mean age and duration of shedding in stool samples ($P = 0.37$).
- > No study detected live virus beyond day 9 of illness, despite persistently high viral loads.
- > There was an association between age >60 years and prolonged viral RNA shedding. Male sex was associated with prolonged SARS-CoV-2 shedding, and the association remained significant even when patients were stratified based on illness severity.
- > Corticosteroid treatment was associated with delayed viral clearance in four studies.
- > No impacts on viral clearance of antiviral regimens/treatment such as remdesivir, or chloroquine, oseltamivir, arbidol, and lopinavir–ritonavir.
- > SARS-CoV-2 viral load in the upper respiratory tract peaked in the 1st week of illness, whereas SARS-CoV peaked at days 10-14 and MERS-CoV peaked at days 7-10.
- > Conclusion: the duration of the viable virus is relatively short - SARS-CoV-2 titres in the upper respiratory tract peak in the first week of illness. Isolation practices should be commenced with the start of the first symptoms to effectively contain SARS-CoV-2.

Reviewed by: Dr Lien Anh Ha Do

Victoria Ivankovic – 3rd Year Medical Student, University of Ottawa

Transmission of SARS-CoV-2 infection by children: a study of contacts of index paediatric cases in India

<https://academic.oup.com/tropej/advance-article/doi/10.1093/tropej/fmaa081/6024862>

- > The susceptibility of children to COVID-19 and the transmission of COVID-19 from children is a relatively unexplored area, and so, the aim of this retrospective observational study was to understand the transmission dynamics in children. As part of state protocol during May 2020, all asymptomatic travellers (adult and children) from states with a high incidence of COVID-19 were institutionally quarantined and tested for COVID-19. Resource constraints prioritised child (< 18 years) COVID-19 testing, and if positive, was considered an index case. Immediate family members (parents and siblings) were subsequently identified as primary contacts and tested accordingly.
- > Paediatric index cases were admitted to hospital, and if less than 15 years of age, were accompanied by a parent - due to resource limitations, no personal protective equipment (PPE) was provided to the parent in the hospital with a COVID-19 positive child; if parents ended up testing positive for COVID-19, they too would be managed according to institutional guidelines.
- > All paediatric index cases and their primary contacts during the month of May 2020 were included in the study; there were 19 index cases in total with a median age of the index child at six years.
 - A total of 42 primary familial contacts (36 adults, six children) with a similar history of travel were identified, along with 80 non-familial contacts.
 - 21 non-familial travellers stayed in the same quarantine institution/room with the identified index cases.
- > The median number of people travelling together was 5, and the mean hours of travel in the same vehicle was 22.8 +/- 9.1 hours, the mean number of people staying in the same room during the quarantine was 4.6 +/- 2.
- > None of the index children or the contacts were in contact with a symptomatic patient before travelling.
- > Of all the primary family contacts, only 5 (11.9%) adult patients tested positive for COVID-19, with all but one remaining asymptomatic during the disease course.
- > Amongst the families included in this study, all who had a similar history of exposure to COVID-19, children more commonly tested positive for the virus.
- > Despite the adults travelling in the same vehicle with their COVID-positive child/children, staying in the same room during the mandatory quarantine period, and in the hospital (without adequate PPE), most of the parents involved in such index cases remained COVID-19 negative.

Reviewed by: Dr Lien Anh Ha Do

Batsho Mandlebe - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

SARS-CoV-2 setting specific transmission rates: a systematic review and meta-analysis

<https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-38-transmission/>

- > This is a systematic review and meta-analysis of the rates of transmission of SARS-CoV-2 in different settings including households, schools, workplaces and healthcare facilities.
- > 97 studies were included in the quantitative synthesis and of those 45 were included in the meta-analysis.
 - Household (29 studies): A pooled estimate of household secondary attack rate (SAR) was 21.1%, and the observed reproduction number (Robs) was 0.96. SAR increased with longer duration of exposure (14.8% with ≤5 days exposure to a household index case vs 28.3% with >5 days exposure).
 - Workplace (7 studies): The pooled SAR estimate when cluster investigations were excluded was 12.3%.
 - Healthcare facilities (28 studies): The pooled estimate SAR was 3.6%. No differences were noted between patient and healthcare staff contact subgroups.
 - Social settings (22 studies): Low SARs were observed in low-contact events with casual contacts or strangers compared to familiar and prolonged contact (1.2% vs 5.9%). However, travel-related contacts had an estimated SAR of 5.0%.
- > Across exposure locations, no significant differences in SAR and the observed reproduction number of index cases aged under 20 and those over 20 were noted. Age-dependent effects in transmissibility and susceptibility remain unknown.
- > Pre-symptomatic and symptomatic index cases had higher SAR rates (9.3% and 12.8%).
- > Estimates of SAR for asymptomatic index cases were approximately two-thirds of those for symptomatic index (3.5% vs. 12.8%).
- > Moderate evidence for less transmission both from and to individuals under 20 years of age in the household context, but this difference is less evident when examining all settings.
- > Contact tracing and isolation activities are an effective measure of reducing onward transmission, as shown by the relatively low Robs across settings.
- > Limitations: data was collected from multiple teams in different countries with varying protocols; reporting and recall biases were reported in several of the included studies; symptomatic cases were more likely to present for medical attention and therefore may be overrepresented in the data; most of the pooled estimates came from China; data pertaining to a large outbreak in care -homes, schools, workplaces and hospitals are still emerging and cannot be systematically searched or reliably cited yet.

- > Conclusion: Transmission of SARS-CoV-2 appears to be highest in environments where prolonged contacts are made (e.g., households and residential locations). However, prolonged social interactions appear to drive onward transmission of SARS-CoV-2. Differences observed in transmissibility by symptom status of index cases and the potential for age-dependent effects has important implications for outbreak control strategies such as contact tracing, testing and rapid isolation of cases.

Reviewed by: Professor Fiona Russell

Thang Dao - 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

A meta-analysis on the role of children in SARS-CoV-2 in household transmission clusters

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1825/6024998>

- > This meta-analysis aimed to address children's role in SARS-CoV-2 transmission in household transmission clusters.
- > The authors investigated the prevalence of paediatric index cases in household transmission clusters of SARS-CoV-2 and the secondary attack rate of different age groups.
 - A household transmission cluster was a group of ≥ 2 confirmed cases in cohabiting individuals in whom the diagnosis of cases occurred within two weeks of each other.
 - The index case was the individual in the household cluster that first developed symptoms.
 - Household secondary attack rates the proportion of confirmed infections among all cohabiting individuals (family members, close relatives, housemates, or house helpers).
- > Using designated search terms and six databases between 1st December 2019 and 24th August 2020, the authors identified 1208 articles. After assessing for eligibility, they included 57 studies in the review.
- > Children were infrequently the index case of household transmission clusters, at only 3.8% of the clusters.
- > Asymptomatic index cases were associated with a significantly lower secondary attack in contacts than symptomatic index cases (estimate risk ratio [R.R.], 0.17 [95% CI 0.09-0.29]).
- > Children have a significantly lower secondary attack rate than adults in household transmission clusters (RR 0.62 [95% CI 0.42-0.91]).
 - Younger children (10 years) were no more or less susceptible to infection compared to older children (>10 years).
- > Implications: During lockdowns that keep schools open, should children become infected at school, they are unlikely to spread SARS-CoV-2 to their cohabiting family members.
- > Limitations of the meta-analysis were:
 - Limited number of included studies and high heterogeneity due to conservative data collection.

- It assumed direct transmission events of infected individuals to the household contacts. However, the household contacts may have acquired the virus from another source (e.g., community exposure), and the first in the family to develop symptoms were not necessarily the index case.
 - It did not control the chance of the same source, whereby two individuals were infected at the same time. Therefore, one individual was incorrectly identified as the sole index case of the cluster as they were the first to develop symptoms.
 - They were unable to differentiate between pre-symptomatic and asymptomatic infections, leading to overestimation of asymptomatic cases.
 - The data should not be extrapolated to transmission outside the home where children can make more social contacts than adults.
- > In conclusion, the data have important implications for the ongoing management of the COVID-19 pandemic.

Reviewed by: Professor Fiona Russell

VACCINES

Australian Government COVID-19 vaccines hub

<https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines-hub>

Chan Ying Zhen Charissa - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

The durability of responses after SARS-CoV-2 mRNA-1273 vaccination

<https://www.nejm.org/doi/full/10.1056/NEJMc2032195>

- > Trial of messenger RNA vaccine, mRNA-1273 to prevent infection with SARS-CoV-2.
- > Immunogenicity data 119 days after first vaccination (90 days after second vaccination).
- > 34 healthy adult participants who received two injections of vaccine at dose of 100µg.
- > mRNA-1273 produced high levels of binding and neutralising antibodies that declined slightly over time but remained elevated in all participants 3 months after booster vaccination.
- > Serum neutralising antibodies continued to be detected in all participants on day 119.
- > No serious adverse events were noted in the trial, no prespecified trial-halting rules were met, and no new adverse events were considered by investigators to be related to vaccine occurred after day 57.
- > Findings provide support for the use of a 100µg dose of mRNA-1273 in ongoing phase 3 trial which has recently shown a 94.5% efficacy rate in the interim analysis.

Reviewed by: Professor Jim Buttery

Dan Lindholm - 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled phase 2/3 trial

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32466-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32466-1/fulltext)

- > This RCT aimed to expand safety and efficacy data for the ChAdOx1 COVID-19 vaccine candidate in 560 individuals, including healthy older adults >70 years of age (n=240).
- > Adverse reactions were common, especially local reactions after dose one, mostly mild and were less common in older people compared to younger participants.
- > Robust antibody (including neutralising antibody) and t-cell immune responses were documented across all age groups who received both a prime and booster dose of the vaccine, regardless of vaccine dose.

- > Whilst correlates of protection against COVID-19 remain unknown, this candidate's tolerable safety profile and induction of significant immune responses in older adults are promising.

Reviewed by: Professor Jim Buttery

Dan Lindholm - 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Ensuring equitable access to COVID-19 vaccines

<https://www.who.int/bulletin/volumes/98/12/20-021220.pdf?ua=1>

- > Despite the impressive COVAX initiative aiming to make two billion doses of COVID-19 vaccines available to low- and middle-income countries in 2021, substantial challenges remain in ensuring equitable access to COVID-19 vaccines.
- > Whilst massive global manufacturing is already underway, countries hoarding vaccines for their use poses one threat to this goal.
- > COVAX also offers the opportunity for pooled procurement of vaccines which would bring vaccine prices down. However, the secretive negotiations of bilateral deals by countries who are not part of this alliance compromises this bargaining power, further threatening equitable access.
- > Gavi, the vaccine alliance, has installed almost 50000 vaccine refrigerators over the last five years, but it is likely that the cold-chain requirements for many of the vaccine candidates will pose a massive challenge to countries without well-established distribution infrastructure.
- > Further stability data at -20 and 4-8°C for mRNA vaccines will be critical to understanding feasibility for these vaccines in many settings.
- > Should the global public health community come together, it is likely that these potentially overwhelming challenges could instead be overcome. However, superpowers like the USA who have not joined COVAX and pursue their own vaccine access deals have the capacity to undermine such impressive global solidarity.

Reviewed by: Professor Jim Buttery

Nicholas Baxter - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Safety and Efficacy of the BNT162b2 mRNA COVID-19 vaccine

<https://www.nejm.org/doi/full/10.1056/NEJMoa2034577>

- > This study describes Phase 2 and 3 results on the safety, immunogenicity, and Efficacy of 30 ug of BNT162b2 or Pfizer/BioNTech vaccine.
- > Lipid nanoparticle-formulated, nucleoside-modified RNA (modRNA) encoding the SARS-CoV-2 full-length spike, modified by two proline mutations to lock it in the perfusion conformation.
- > PICO:
 - Population: healthy adults 16 years or older or adults who had stable chronic medical conditions, including HIV, Hep B and Hep C. Patients were excluded with a medical history of COVID-19 or treatment with immunosuppressive therapy, or a diagnosis with an immunocompromising condition.

- Intervention: two 30ug doses of BNT162b2 administered intramuscularly 21 days apart
- Comparator: placebo
- Outcomes:
 - Safety - Specific local adverse events, use of antipyretic or pain medication, within seven days after the receipt of each dose of vaccine or placebo.
 - Efficacy - Endpoints included Efficacy against confirmed COVID-19 with onset at least seven days after the second dose, and Efficacy in participants with and without evidence of prior infection, and Efficacy against severe COVID-19.

> Results:

- Adverse events were more common after dose two and were predominantly systemic reactogenicity.
- Systemic reactogenic events were reported more often by younger vaccine recipients (16 to 55 years of age) than older vaccine recipients (older than 55 years of age).
- Most commonly reported systemic events included fatigue (59%) and headache (52%) in younger participants, and 51% and 39% among older recipients.
- Fever (>38°C) was reported after the second dose by 16% of younger vaccine recipients and by 11% of older recipients.
- Younger vaccine recipients were more likely to use antipyretic or pain medication (28% after dose one, 45% after dose two) than older recipients (20% after dose one, 38% after dose two). Placebo recipients were less likely to use medications, regardless of age or dose.
- More BNT162b2 recipients than placebo recipients reported any adverse event (27% vs 12%), which primarily reflects the inclusion of transient reactogenicity events.
- Sixty-four vaccine recipients (0.3%) and 6 placebo recipients (<0.1%) reported lymphadenopathy.
- Few participants in either group had severe adverse events, serious adverse events, or adverse events leading to withdrawal from the trial.
- Two BNT162b2 recipients died as did four placebo recipients from unrelated causes. No deaths were considered by the investigators to be related to the vaccine or placebo.
- Among 36,523 participants who had no evidence of existing or prior SARS-CoV-2 infection, 8 cases of COVID-19 within onset at least seven days after the second dose were observed among vaccine recipients and 162 among placebo recipients. This case split corresponds to 95.0% vaccine efficacy (CI 90.3 to 97.6).
- Between the first dose and the second dose, 39 cases in the BNT162b2 group and 82 cases in the placebo group were observed, resulting in a single dose vaccine efficacy of 52% (29.5% to 68.4%).

- > Conclusions:
 - A two-dose regimen of BNT162b2 (30 ug per dose, given 21 days apart) was found to be safe and 95% effective against COVID-19.
 - The vaccine met both primary and secondary efficacy endpoints, with more than a 99.99% probability of a true vaccine efficacy greater than 30%.

Reviewed by: Professor Jim Buttery

Chelsea Haliburton – 3rd Year Medical Student, University of Ottawa

Moderna announces primary efficacy analysis in Phase 3 of COVE Study for its COVID-19 vaccine candidate and filing today with the U.S. FDA for emergency use authorisation

<https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-primary-efficacy-analysis-phase-3-cove-study>

- > Press release by the manufacturer.
- > Primary endpoint analysed confirmed COVID-19 cases and adjudicated starting two weeks following the second dose of the vaccine.
- > Secondary endpoint analysed severe cases of COVID-19.
- > 30 000 participants.
 - 195 cases of COVID-19; 30 of which were severe.
 - 185 cases in the placebo group (including all 30 severe cases).
 - 11 cases in the active treatment group.
- > Vaccine efficacy against COVID-19 was 94.1%; vaccine efficacy against severe COVID-19 infection was 100%.
- > Efficacy was consistent across age, race, ethnicity and gender demographics.
- > Most common adverse effects from the vaccine: injection site pain, fatigue, myalgia, arthralgia, headache and erythema at the injection site.
- > Vaccine trial as passed the two months of medial follow-up post-vaccination required by FDA for emergency use authorisation.
- > Safety data continues to be monitored, and no serious safety concerns have been identified to date.

Reviewed by: Professor Jim Buttery

VIROLOGY

Angela Zhu - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in the severity of SARS-CoV-2 infections
<https://adc.bmj.com/content/early/2020/11/30/archdischild-2020-320338>

- > This article reviews the proposed hypotheses accounting for age-related differences in COVID-19 severity.
- > Children infected with SARS-CoV-2 typically have reduced severity, need for hospitalisation and mortality compared to older adults, which surprisingly, is the opposite of most other respiratory viruses.
- > Risk of infection following contact with SARS-CoV-2-positive cases may be lower in children, as supported by the rarity of transmission within schools. However, emerging evidence suggests that infected children carry similar viral loads to adults.
- > Factors that increase infection risk in adults include:
 - Age-dependent endothelial damage and hypercoagulable state.
 - Increased ACE2 receptors and TMPRSS2 expression with age facilitate virus entry into cells.
 - Increased non-neutralising HCoV antibody-dependent enhancement.
 - Increased immunosenescence and inflammaging.
 - Increased prevalence of comorbidities and smoking.
 - Reduced levels of anti-inflammatory and anti-oxidative agents such as vitamin D.
- > Factors that protect children include:
 - Age-related differences in innate and adaptive immune responses.
 - Coinfection with common childhood pathogens enhances SARS-CoV-2 clearance.
 - Differences in the microbiota.
 - Increased melatonin levels.
 - Off-target effects of live vaccines, e.g., BCG and measles-containing vaccines.
 - Reduced-intensity of exposed viral loads.
- > In conclusion, the exact mechanism behind the reduced severity of COVID-19 in children remains unclear. Unravelling this will provide insights into prevention and treatment strategies.

Reviewed by: Dr Celeste Donato

OTHER RESOURCES

All COVID-19 literature

<https://www.ncbi.nlm.nih.gov/research/coronavirus/>

A pandemic primer on excess mortality statistics and their comparability across countries

<https://ourworldindata.org/covid-excess-mortality>

Australian Government Department of Health Webinars on the COVID-19 response for primary care practitioners

<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-advice-for-the-health-and-aged-care-sector/webinars-on-the-coronavirus-covid-19-response-for-primary-care-practitioners>

Australian Government

<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers>

<https://www.health.gov.au/resources/publications/management-and-operational-plan-for-people-with-disability>

Burnet Institute research findings, policy and technical reports

https://www.burnet.edu.au/covid-19//36_know_c19_hub

COVID-19 and the kidney, currently the recommended U.S. resource

<http://www.nephjc.com/covid19>

Daily updates on COVID-19 literature compiled by Canadian medical students

https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuLV0aJdf_z2uWV7r3FaPzAO86q9ZXBcTZ1OcCE_Nw/formResponse

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects

<https://dontforgetthebubbles.com/evidence-summary-paediatric-covid-19-literature/>

Global summary, identifying changes in the reproduction number, rate of spread, and doubling time during the course of the COVID-19 outbreak whilst accounting for potential biases due to delays in case reporting both nationally and sub-nationally

<https://epiforecasts.io/covid/posts/global/>

Introduction to Coronavirus: free, online course aimed at teenagers and young adults: scientists and experts from the London School of Hygiene & Tropical Medicine explain research to understand the virus and guide the global response to coronavirus

<https://www.open.edu/openlearncreate/course/view.php?id=5319>

Lancet COVID-19 papers

https://www.thelancet.com/coronavirus?utm_campaign=tlcoronavirus20&utm_content=126383502&utm_medium=social&utm_source=twitter&hss_channel=tw-27013292

National COVID-19 clinical evidence taskforce: continually updated evidence-based clinical guidelines

<https://covid19evidence.net.au/>

Our world in data: statistics and research: Coronavirus pandemic (COVID-19)

<https://ourworldindata.org/coronavirus>

Oxford COVID-19 Evidence Service

<https://www.cebm.net/oxford-covid-19/>

Public Health England COVID-19 Rapid Reviewed - Knowledge & Library Service

<https://phelibrary.koha-ptfs.co.uk/covid19rapidreviews/>

Retracted coronavirus (COVID-19) papers

<https://retractionwatch.com/retracted-coronavirus-covid-19-papers/>

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)

<https://www.scimex.org/info/2019-20-coronavirus>

<https://www.covid19-hpc-consortium.org/>

University of Birmingham COVID-19 Research Briefing

<https://www.birmingham.ac.uk/university/colleges/mds/Coronavirus/COVID-19-research-briefing.aspx>

Victorian Department of Health and Human Services

<https://www.dhhs.vic.gov.au/coronavirus-covid-19-daily-update>

WHO Rolling updates on COVID-19

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>

WHO COVID-19 dashboard

<https://covid19.who.int/>

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